

X-16438.ST25.txt
SEQUENCE LISTING

<110> Eli Lilly and Company
<120> USES OF MELANOCORTIN-4 RECEPTOR (MC4R) AGONIST PEPTIDES
ADMINISTERED BY CONTINUOUS INFUSION
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<150> US 60/557347
<151> 2004-03-29
<150> US 60/570676
<151> 2004-05-13
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X-16438.ST25.txt

<223> D form

<220>

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<222> (7)..(7)

<223> AMIDATION

<400> 42

Cys Glu His Phe Arg Trp Cys
1 5

<210> 43

<211> 7

<212> PRT

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<223> acetyl-diaminopropionyl substituted

<220>

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<220>

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<223> D form

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<223> AMIDATION

<400> 43

Cys Glu His Phe Arg Trp Cys
1 5

<210> 44

<211> 7

<212> PRT

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<223> acetyl-diaminobutyryl substituted

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X-16438.ST25.txt

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<223> AMIDATION

<400> 44

Cys Glu His Phe Arg Trp Cys
1 5

<210> 45

<211> 8

<212> PRT

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<220>

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<222> (5)..(5)

<223> D form

<400> 45

Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 46

<211> 8

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X-16438.ST25.txt

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<223> AMIDATION

<400> 46

Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 47

<211> 8

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<222> (2)..(8)

<220>

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<223> AMIDATION

<400> 47

Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 48

<211> 8

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X-16438.ST25.txt

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Arg Cys Glu His Phe Arg Trp Cys
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<210> 49

<211> 8

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<220>

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<220>

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<222> (5)..(5)

<223> D form

<400> 49

Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 50

<211> 8

<212> PRT

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X-16438.ST25.txt

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<220>

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<223> 4-chloro substituted, D form

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<223> AMIDATION

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Arg Cys Glu His Phe Arg Trp Cys
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<210> 51

<211> 8

<212> PRT

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<223> 1-methyl substituted

<220>

<221> MOD_RES

<222> (5)..(5)

<223> D form

<220>

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<223> AMIDATION

<400> 51

Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 52

<211> 8

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct X-16438.ST25.txt

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<400> 52

Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 53
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<220>
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<400> 53

X-16438.ST25.txt
Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 54
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<223> Xaa = homoarginine

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<220>
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<223> D form

<220>
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<222> (8)..(8)
<223> AMIDATION

<400> 54

Xaa Cys Glu His Phe Arg Trp Cys
1 5

<210> 55
<211> 8
<212> PRT
<213> Artificial

<220>
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<223> ACETYLTATION

<220>
<221> MISC_FEATURE
<222> (1)..(1)
<223> Xaa = citrulline

<220>

X-16438.ST25.txt

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<220>
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<223> D form

<220>
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<223> AMIDATION

<400> 55

Xaa Cys Glu His Phe Arg Trp Cys
1 5

<210> 56
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<220>
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<223> D form

<220>
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<222> (8)..(8)
<223> AMIDATION

<400> 56

Xaa Cys Glu His Phe Arg Trp Cys
1 5

X-16438.ST25.txt

<210> 57
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<212> PRT
<213> Artificial

<220>
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<400> 57

Leu Cys Glu His Phe Arg Trp Cys
1 5

<210> 58
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<212> PRT
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<223> AMIDATION

<400> 58

X-16438.ST25.txt

Lys Cys Glu His Phe Arg Trp Cys
1 5

<210> 59
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<223> Xaa = N(epsilon)-isopropyl lysine

<220>
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<223> D form

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<223> AMIDATION

<400> 59

Xaa Cys Glu His Phe Arg Trp Cys
1 5

<210> 60
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X-16438.ST25.txt

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 <223> D form

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Xaa Cys Glu His Phe Arg Trp Cys
 1 5

<210> 61
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 <223> Xaa = norleucine

<220>
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 <223> D form

<220>
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 <223> AMIDATION

<400> 61

Xaa Cys Glu His Phe Arg Trp Cys Ser Pro
 1 5 10

<210> 62
 <211> 8
 <212> PRT
 <213> Artificial

X-16438.ST25.txt

<220>
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<223> Xaa = Ornithine

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<400> 62

Xaa Cys Glu His Phe Arg Trp Cys
1 5

<210> 63
<211> 8
<212> PRT
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<220>
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<223> D form

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X-16438.ST25.txt

<400> 63

Val Cys Glu His Phe Arg Trp Cys
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<210> 64

<211> 8

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

<220>

<221> MOD_RES

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<223> N-(2-naphthalenesulfonyl) substituted, D form

<220>

<221> DISULFID

<222> (2)..(8)

<220>

<221> MOD_RES

<222> (5)..(5)

<223> D form

<220>

<221> MOD_RES

<222> (8)..(8)

<223> AMIDATION

<400> 64

Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 65

<211> 8

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

<220>

<221> MOD_RES

<222> (1)..(1)

<223> N-(2-naphthalenesulfonylamino-4-oxo-butyryl) substituted, D form

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<222> (2)..(8)

<220>

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<223> D form

X-16438.ST25.txt

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<223> AMIDATION

<400> 65

Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 66
<211> 8
<212> PRT
<213> Artificial

<220>
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<223> 3-(4-hydroxyphenyl)propionyl substituted

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<223> D form

<220>
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<223> AMIDATION

<400> 66

Arg Cys Glu His Phe Arg Trp Cys
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<210> 67
<211> 8
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X-16438.ST25.txt

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<223> D form

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<400> 67

Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 68
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<223> D form

<220>
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<223> AMIDATION

<400> 68

Tyr Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 69
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<212> PRT
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<220>
<221> MOD_RES
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<223> D form

X-16438.ST25.txt

<400> 69

Tyr Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 70

<211> 9

<212> PRT

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<220>

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<223> D form

<220>

<221> MOD_RES

<222> (9)..(9)

<223> NH-(CH₂)₆-NH₂ substituted

<400> 70

Tyr Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 71

<211> 10

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

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<223> D form

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<222> (10)..(10)

<223> AMIDATION

<400> 71

Tyr Arg Cys Glu His Phe Arg Trp Cys Glu
1 5 10

X-16438.ST25.txt

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<400> 72
Tyr Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 73
<211> 9
<212> PRT
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<220>
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<220>
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<223> D form

<400> 73
Tyr Arg Cys Glu His Phe Arg Trp Cys
1 5

X-16438.ST25.txt

<210> 74
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<220>
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<400> 74

Tyr Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 75
<211> 9
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<220>
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<220>
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<220>
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X-16438.ST25.txt

<400> 75

Tyr Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 76

<211> 9

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

<220>

<221> MOD_RES

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<223> N-glutaryl substituted

<220>

<221> DISULFID

<222> (3)..(9)

<220>

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<222> (6)..(6)

<223> D form

<400> 76

Tyr Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 77

<211> 9

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

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<223> gluconoyl substituted

<220>

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<223> D form

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<222> (9)..(9)

<223> AMIDATION

X-16438.ST25.txt

<400> 77

Tyr Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 78

<211> 9

<212> PRT

<213> Artificial

<220>

<223> synthetic construct

<220>

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<222> (3)..(9)

<220>

<221> MOD_RES

<222> (6)..(6)

<223> D form

<220>

<221> MOD_RES

<222> (9)..(9)

<223> Reduced from amino acid to amino alcohol

<400> 78

Tyr Arg Cys Glu His Phe Arg Trp Xaa
1 5

<210> 79

<211> 9

<212> PRT

<213> Artificial

<220>

<223> synthetic construct

<220>

<221> MOD_RES

<222> (1)..(1)

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<220>

<221> MOD_RES

<222> (2)..(2)

<223> D form

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<221> DISULFID

<222> (3)..(9)

X-16438.ST25.txt

<220>

<221> MOD_RES

<222> (6)..(6)

<223> D form

<220>

<221> MOD_RES

<222> (9)..(9)

<223> AMIDATION

<400> 79

Tyr Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 80

<211> 9

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

<220>

<221> MOD_RES

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<222> (3)..(3)

<223> D form

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<221> MOD_RES

<222> (6)..(6)

<223> D form

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<221> MOD_RES

<222> (9)..(9)

<223> AMIDATION

<400> 80

Tyr Arg Cys Glu His Phe Arg Trp Cys
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<210> 81

<211> 9

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

X-16438.ST25.txt

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<222> (5)..(5)
<223> 1-methyl substituted

<220>
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<223> AMIDATION

<400> 81

Tyr Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 82
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<220>
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<223> 1-methyl substituted, D form

<220>
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<223> D form

<220>
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X-16438.ST25.txt

<400> 82

Tyr Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 83

<211> 9

<212> PRT

<213> Artificial

<220>

<223> synthetic construct

<220>

<221> MOD_RES

<222> (1)..(1)

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<220>

<221> DISULFID

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<220>

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<222> (6)..(6)

<223> 4-fluoro substituted, D form

<220>

<221> MOD_RES

<222> (9)..(9)

<223> AMIDATION

<400> 83

Tyr Arg Cys Glu His Phe Arg Trp Cys
1 5

<210> 84

<211> 9

<212> PRT

<213> Artificial

<220>

<223> synthetic construct

<220>

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<222> (1)..(1)

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<222> (3)..(9)

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X-16438.ST25.txt

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1 5

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X-16438.ST25.txt

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X-16438.ST25.txt

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X-16438.ST25.txt

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 1 5

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X-16438.ST25.txt

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1 5

X-16438.ST25.txt

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X-16438.ST25.txt

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X-16438.ST25.txt

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X-16438.ST25.txt

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1 5

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X-16438.ST25.txt

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X-16438.ST25.txt

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<222> (10)..(10)

<223> reduced from amino acid to amino alcohol

<400> 116

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<220>

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<223> D form

<220>

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<223> NH-(CH₂)₆-NH₂ substituted

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1				5				

X-16438.ST25.txt

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X-16438.ST25.txt

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<222> (11)..(11)

<223> reduced from amino acid to amino alcohol

<400> 120

Tyr Arg Cys Glu His Phe Arg Trp Cys Ser Xaa
 1 5 10

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X-16438.ST25.txt

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<400> 122

Tyr Arg Cys Glu His Phe Arg Trp Cys Lys Xaa
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X-16438.ST25.txt

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X-16438.ST25.txt

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X-16438.ST25.txt

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Tyr Xaa Cys Glu His Phe Arg Trp Cys
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Tyr Xaa Cys Glu His Phe Arg Trp Cys
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X-16438.ST25.txt

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X-16438.ST25.txt

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X-16438.ST25.txt

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X-16438.ST25.txt

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X-16438.ST25.txt

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5

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<223> Xaa = homocysteine

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X-16438.ST25.txt

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Xaa His Phe Arg Trp Cys
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<220>

<221> MOD_RES

<222> (3)..(3)

<223> D form

<400> 138

Xaa His Phe Arg Trp Cys
1 5

<210> 139

<211> 6

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X-16438.ST25.txt

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X-16438.ST25.txt

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X-16438.ST25.txt

<223> AMIDATION

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Xaa His Phe Arg Trp Cys
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<210> 144

<211> 6

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X-16438.ST25.txt

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<223> AMIDATION

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<210> 145

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<223> D form

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<223> AMIDATION

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Xaa His Phe Arg Trp Cys
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<210> 146

X-16438.ST25.txt

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Xaa His Phe Arg Trp Cys
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1 5

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X-16438.ST25.txt

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X-16438.ST25.txt

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X-16438.ST25.txt

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<400> 152

Xaa His Phe Arg Trp Cys
 1 5

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Arg Xaa His Phe Arg Trp Cys
 1 5

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X-16438.ST25.txt

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Arg Xaa His Phe Arg Trp Cys
1 5

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<223> D form

<400> 155

Arg Xaa His Phe Arg Trp Cys
1 5

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X-16438.ST25.txt

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Arg Xaa His Phe Arg Trp Cys .
1 5

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<220>
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<223> D form

X-16438.ST25.txt

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Arg Xaa His Phe Arg Trp Cys
1 5

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X-16438.ST25.txt

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Arg Xaa His Phe Arg Trp Cys
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X-16438.ST25.txt

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Xaa Xaa His Phe Arg Trp Cys
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X-16438.ST25.txt

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Tyr Arg Xaa His Phe Arg Trp Cys
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Tyr Arg Xaa His Phe Arg Trp Cys
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Tyr Arg Xaa His Phe Arg Trp Cys
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X-16438.ST25.txt

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Xaa His Ala Arg Trp Cys
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<223> D form

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<223> AMIDATION

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<223> Xaa = penicillamine

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Xaa His Phe Arg Trp Xaa
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<210> 169

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Xaa His Phe Arg Trp Xaa
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Xaa His Phe Arg Trp Xaa
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Xaa His Phe Arg Trp Xaa
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X-16438.ST25.txt

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Xaa His Phe Arg Trp Xaa
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X-16438.ST25.txt

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Xaa His Phe Arg Trp Xaa
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Xaa His Phe Arg Trp Xaa
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X-16438.ST25.txt

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X-16438.ST25.txt

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Xaa His Phe Arg Trp Xaa
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X-16438.ST25.txt

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Xaa Xaa His Phe Arg Trp Xaa
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Gly Xaa His Phe Arg Trp Xaa
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X-16438.ST25.txt

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Xaa His Phe Arg Trp Xaa
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Cys His Phe Arg Trp Xaa

1 5 X-16438.ST25.txt

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Cys His Phe Arg Trp Xaa
1 5

<210> 182
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X-16438.ST25.txt

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Cys His Phe Arg Trp Xaa
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Cys His Phe Arg Trp Xaa
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X-16438.ST25.txt

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Cys His Phe Arg Trp Xaa
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Cys His Phe Arg Trp Xaa
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X-16438.ST25.txt

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Arg Cys His Phe Arg Trp Xaa
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<400> 187

Arg Cys His Phe Arg Trp Xaa X-16438.ST25.txt
1 5

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Arg Cys His Phe Arg Trp Xaa
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X-16438.ST25.txt

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 Arg Cys His Phe Arg Trp Xaa
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Arg Cys His Phe Arg Trp Xaa
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X-16438.ST25.txt

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Arg Cys His Phe Arg Trp Xaa
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X-16438.ST25.txt

Tyr Arg Cys Glu His Phe Arg Trp Xaa
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Xaa His Phe Arg Trp Xaa
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X-16438.ST25.txt

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<222> (7)..(7)
<223> Xaa = homocysteine

<400> 194

Arg Xaa His Phe Arg Trp Xaa
1 5

<210> 195
<211> 7
<212> PRT
<213> Artificial

<220>
<223> Synthetic construct

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLATION

<220>
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<222> (2)..(7)

<220>
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<222> (2)..(2)
<223> Xaa = homocysteine

<220>
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<222> (4)..(4)
<223> D form

<220>
<221> MOD_RES
<222> (7)..(7)
<223> AMIDATION

<220>
<221> MISC_FEATURE
<222> (7)..(7)
<223> Xaa = homocysteine

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<400> 195

Arg Xaa His Phe Arg Trp Xaa
 1 5

<210> 196

<211> 8

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

<220>

<221> MOD_RES

<222> (1)..(1)

<223> ACETYLTATION

<220>

<221> DISULFID

<222> (3)..(8)

<220>

<221> MISC_FEATURE

<222> (3)..(3)

<223> Xaa = homocysteine

<220>

<221> MOD_RES

<222> (5)..(5)

<223> D form

<220>

<221> MOD_RES

<222> (8)..(8)

<223> AMIDATION

<220>

<221> MISC_FEATURE

<222> (8)..(8)

<223> Xaa = homocysteine

<400> 196

Tyr Arg Xaa His Phe Arg Trp Xaa
 1 5

<210> 197

<211> 9

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

<220>

<221> MOD_RES

<222> (1)..(1)

<223> ACETYLTATION

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<220>
<221> DISULFID
<222> (3)..(9)

<220>
<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa = homocysteine

<220>
<221> MOD_RES
<222> (6)..(6)
<223> D form

<220>
<221> MOD_RES
<222> (9)..(9)
<223> AMIDATION

<220>
<221> MISC_FEATURE
<222> (9)..(9)
<223> Xaa = homocysteine

<400> 197
Tyr Arg Xaa Glu His Phe Arg Trp Xaa
1 5

<210> 198
<211> 6
<212> PRT
<213> Artificial

<220>
<223> synthetic construct

<220>
<221> MOD_RES
<222> (1)..(1)
<223> ACETYLTATION

<220>
<221> DISULFID
<222> (1)..(6)
<223> S-CH₂-S linkage

<220>
<221> MOD_RES
<222> (3)..(3)
<223> D form

<220>
<221> MOD_RES
<222> (6)..(6)
<223> AMIDATION

<400> 198
Cys His Phe Arg Trp Cys

X-16438.ST25.txt

1

5

<210> 199
 <211> 9
 <212> PRT
 <213> Artificial

<220>
 <223> synthetic construct

<220>
 <221> MISC_FEATURE
 <222> (1)..(1)
 <223> Xaa = Arg, Tyr-Arg, Tyr-beta-Arg, or is absent

<220>
 <221> MISC_FEATURE
 <222> (1)..(1)
 <223> Xaa = a modified amino acid including Arg, citrulline, homoarginine, Leu, Lys, N-isopropyl-Lys, norleucine, ornithine, or Val

<220>
 <221> MISC_FEATURE
 <222> (1)..(1)
 <223> Xaa = a modified group including Tyr-Arg, Tyr-citrulline, Cya-Arg, Tyr-homoarginine, Tyr-l-beta-homoarginine, Tyr-Lys, Tyr-Ser, or Tyr-Val

<220>
 <221> DISULFID
 <222> (2)..(8)
 <223> S-S or S-CH₂-S disulfide bridge

<220>
 <221> MISC_FEATURE
 <222> (2)..(2)
 <223> Xaa = Cys, homocysteine, or desamino-cysteine; may be D or L form

<220>
 <221> MISC_FEATURE
 <222> (3)..(3)
 <223> Xaa = Glu, Gln, Asp, Asn, Ala, Gly, Thr, Ser, Pro, Met, Ile, Val, Arg, His, Tyr, Trp, Phe, Lys, Leu, cysteic acid, or is absent

<220>
 <221> MISC_FEATURE
 <222> (4)..(4)
 <223> Xaa = His, modified His, or modified Ala; D or L form

<220>
 <221> MISC_FEATURE
 <222> (5)..(5)
 <223> Xaa = Phe, modified Phe, or modified Ala; D or L form

<220>
 <221> MISC_FEATURE
 <222> (6)..(6)
 <223> Xaa = Arg or modified Arg; D or L form

<220>

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<221> MISC_FEATURE

<222> (8)..(8)

<223> Xaa = Cys, homocysteine, or modified cysteine or homocysteine (such as amide, alcohol, or penicillamine)

<220>

<221> MISC_FEATURE

<222> (9)..(9)

<223> Xaa = Ser-Pro-NH₂, Lys-Pro-NH₂, Ser-OH, Ser-Pro-OH, Lys-OH, Ser alcohol, Ser-Pro alcohol, Arg-Phe-NH₂, Glu-NH₂, or is absent

<400> 199

Xaa Xaa Xaa Xaa Xaa Xaa Trp Xaa Xaa
 1 5

<210> 200

<211> 9

<212> PRT

<213> Artificial

<220>

<223> synthetic construct

<220>

<221> MISC_FEATURE

<222> (1)..(1)

<223> Xaa = Arg, Tyr-Arg, Tyr-beta-Arg, or is absent

<220>

<221> MISC_FEATURE

<222> (1)..(1)

<223> Xaa = a modified amino acid including Arg, citrulline, homoarginine, Leu, Lys, N-isopropyl-Lys, norleucine, ornithine, or Val

<220>

<221> MISC_FEATURE

<222> (1)..(1)

<223> Xaa = a modified group including Tyr-Arg, Tyr-citrulline, Cya-Arg, Tyr-homoarginine, Tyr-l-beta-homoarginine, Tyr-Lys, Tyr-Ser, or Tyr-Val

<220>

<221> DISULFID

<222> (2)..(8)

<220>

<221> MISC_FEATURE

<222> (2)..(2)

<223> Xaa = Cys or homocysteine

<220>

<221> MISC_FEATURE

<222> (3)..(3)

<223> Xaa = Glu, Gln, Asp, Asn, Ala, Gly, Thr, Ser, Pro, Met, Ile, Val, Arg, His, Tyr, Trp, Phe, Lys, Leu, cysteic acid, or is absent

<220>

<221> MOD_RES

<222> (4)..(4)

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<223> His may be optionally substituted

<220>

<221> MOD_RES

<222> (5)..(5)

<223> Phe may be optionally substituted

<220>

<221> MISC_FEATURE

<222> (8)..(8)

<223> Xaa = Cys, homocysteine, or modified cysteine or homocysteine such as amide

<220>

<221> MISC_FEATURE

<222> (9)..(9)

<223> Xaa = Ser-Pro-NH₂, Lys-Pro-NH₂, Ser-OH, Ser-Pro-OH, Lys-OH, Ser alcohol, Ser-Pro alcohol, Arg-Phe-NH₂, Glu-NH₂, or is absent

<400> 200

Xaa Xaa Xaa His Phe Arg Trp Xaa Xaa
 1 5

<210> 201

<211> 9

<212> PRT

<213> Artificial

<220>

<223> Synthetic construct

<220>

<221> MISC_FEATURE

<222> (1)..(1)

<223> Xaa = Arg, Tyr-Arg, Tyr-beta-Arg, or is absent

<220>

<221> MISC_FEATURE

<222> (1)..(1)

<223> Xaa = a modified amino acid including Arg, citrulline, homoarginine, Leu, Lys, N-isopropyl-Lys, norleucine, ornithine, or Val

<220>

<221> MISC_FEATURE

<222> (1)..(1)

<223> Xaa = a modified group including Tyr-Arg, Tyr-citrulline, Tyr-homoarginine, Tyr-1-beta-homoarginine, Tyr-Lys, Tyr-Ser, or Tyr-Val

<220>

<221> DISULFID

<222> (2)..(8)

<220>

<221> MISC_FEATURE

<222> (2)..(2)

<223> Xaa = Cys or homocysteine

<220>

X-16438.ST25.txt

<221> MISC_FEATURE
<222> (3)..(3)
<223> Xaa = Glu, Gln, Asp, Asn, Ala, Gly, Thr, Ser, Pro, Met, Ile, Val,
Arg, His, Tyr, Trp, Phe, or is absent

<220>
<221> MOD_RES
<222> (4)..(4)
<223> His may be optionally substituted

<220>
<221> MOD_RES
<222> (5)..(5)
<223> Phe may be optionally substituted

<220>
<221> MISC_FEATURE
<222> (8)..(8)
<223> Xaa = Cys, homocysteine, or modified cysteine or homocysteine
such as amide

<220>
<221> MISC_FEATURE
<222> (9)..(9)
<223> Xaa = Ser-Pro-NH₂, Lys-Pro-NH₂, Ser-OH, Ser-Pro-OH, Lys-Pro-OH,
Arg-Phe-NH₂, Glu-NH₂, or is absent

<400> 201

Xaa Xaa Xaa His Phe Arg Trp Xaa Xaa
1 5